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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,382	07/02/2001	Hiromi Ohtaki	210213US0	1400

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KERR, KATHLEEN M

[REDACTED] ART UNIT [REDACTED] PAPER NUMBER

1652

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/895,382	OHTAKI ET AL.
	Examiner Kathleen M Kerr	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 20 December 2002.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) 5-9 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-4 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) Paper No(s). <u>13</u> . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7,8</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 10, mailed on September 23, 2002), Applicants filed a response received on December 20, 2002 (Paper No. 12). Claims 1-9 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group I, Claims 1-4, and species trehalose-6-phosphate synthase, in Paper No. 12 is acknowledged. The traversal is on the ground(s) that no reasons and/or examples have been provided to support a conclusion of patentably distinctness between the identified Groups. This is not found persuasive because distinctness was, in fact, provided previously. The Examiner had noted the distinctness of the product and process of use Groups (Groups I and II) and the differences between the different product Groups, Groups I, III, and IV. The product Groups are distinct based on distinct structures where Group I is the absence of one or both the genes claimed in Groups III and IV. The genes in Groups III and IV are structurally distinct from each other and encode functionally distinct proteins.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-9 are pending in the instant application. Claims 5-9 are withdrawn from further consideration as non-elected inventions. The Examiner does note that Claim 5 may be subject to rejoinder upon the identification of allowable product claims from Group I. Claims 1-4 will be examined herein.

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Priority

3. The instant application is granted the benefit of priority for the foreign application 2000-204256 filed on July 5, 2000 in Japan as requested in the declaration. The Examiner notes that no English translation has been filed with the U.S. Patent office, thus, the priority date of the foreign application cannot be used when considering prior art.

Information Disclosure Statement

4. The information disclosure statement filed on October 2, 2001 (Paper No. 7) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

No copies of references accompany the information disclosure statement filed on January 11, 2002 (Paper No. 8); thus, its references have not been considered as noted on the attached copy.

Objections to the Specification

5. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Coryneform bacteria with decreased trehalose synthesis ability for the production of glutamic acid---

6. The specification is objected to for lacking consistency in the description of SEQ ID NO:14. On page 25, line 8, SEQ ID NO:14 is described as primer P8 for the otsA gene while on page 26, line 2, SEQ ID NO:14 is described as primer P3 for the treY gene. Clarification is required.

Claim Objections

7. Claims 2 and 3 are objected to for improper language. In each case, the term “trehalose synthesis pathway” should be preceded by an article, such as ---the---. Correction is required.
8. Claim 2 is objected to for a spelling error; in line 4, the term “systhesis” should be ---synthesis---. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of the term “trehalose synthesis pathway” are unclear. On page 9 of the specification, exemplary enzymes are noted, but these do not define the metes and bounds. Must enzymes in this genus directly produce trehalose? particular trehalose precursors? The metes and bounds are unclear. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 is drawn to coryneform bacterium claimed solely by functional limitation; Claim 2 is drawn to coryneform bacterium claimed by functional limitations with an unclear structural limitation; Claim 3 is drawn to coryneform bacterium claimed by functional limitations wherein the structural limitations are not adequately described in view of the described species.

The Court of Appeals for the Federal Circuit has recently held that a “written description of an invention involving a chemical genus, like a description of a chemical species, ‘requires a precise definition, such as be structure, formula [or] chemical name,’ of the claimed subject matter sufficient to distinguish it from other materials.” University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical

characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a knockout construct (plasmid) of the trehalose-6-phosphate synthase gene of *C. glutamicum* bacterium is described. The description of this construct further describes coryneform transformed with this plasmid to produce the claimed invention. In the case of Claims 1 and 2, in which no particular gene knockout is required, the description in the specification is wholly inadequate to support the claimed genus because the knockout constructs described do NOT adequately describe all knockout constructs that would disrupt the trehalose synthesis pathway in structural terms. In fact, no generic structure is described in the specification to describe this genus. In the case of Claim 3, a single species of either knockout plasmid is described; said species would produce knockout *C. glutamicum* (or *B. lactofermentum*, an equivalent species name). However, without knowing the similarity between the *C. glutamicum* sequences and other coryneform sequences, this single species does not adequately describe the claimed genus.

For Claim 3, the Examiner suggests adding definite structural limitations, such as a structural relationship (percent identity) between the trehalose-6-phosphate gene to be knocked out and SEQ ID NO:29.

11. Claims 1-2 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for coryneform bacteria with knocked out trehalose-6-phosphate synthase, does not reasonably provide enablement for coryneform bacteria with trehalose synthesis activity decreased via other means. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

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make the invention commensurate in scope with these claims. To produce the claimed products to the full extent of their extended scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification provides two working examples of coryneform with decreased trehalose synthesis; these examples render the scope of Claims 3 and 4 fully enabled. The specification presents no guidance for the determination of other *genes* whose knock out would decrease coryneform trehalose synthesis. The state of the prior art is that while trehalose biosynthesis has been studies, the effective deletion of the pathway is uncertain. Moreover, the

predictability of other genes whose deletion would have the same result of trehalose synthesis is very low. For these reasons, the instant claims are not enabled to the full extent of their scope.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Claims 1-4 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-4, as written, do not sufficiently distinguish over cells as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. The Examiner notes that the deletions claimed can occur naturally. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated". See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. § 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. § 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

13. Claims 1-4 are rejected under 35 U.S.C. § 102(e) as being anticipated by Pompejus *et al.* (WO 02/05123). The instant claims are drawn to a coryneform bacterium with a deletion of the trehalose-6-phosphate synthase gene, SEQ ID NO:29.

Pompejus *et al.* teach the trehalose-6-phosphate synthase gene of *C. glutamicum* (see SEQ ID NOS: 29 and 30). Pompejus *et al.* also teach the functional disruption of each of their genes taught (23 genes in all, see sequence listing) by homologous recombination (see page 6, lines 30-40). While Pompejus *et al.* has not taught an actual reduction to practice of the claimed invention, Pompejus *et al.* has fully conceived of the claimed invention and has fully enabled the claimed invention.

Additional References

14. The following are cited to complete the record:

- a) Hermann *et al.* US 2002/0192674 A1 published December 19, 2002 teaches a plasmid pK19mobsacBΔotsA for the deletion of trehalose-6-phosphate synthase in *C. glutamicum*.
- b) Gourdon *et al.* Metabolic Analysis of Glutamate Production by *Corynebacterium glutamicum*. Metabolic Engineering (July, 1999) 1:224-231.

Conclusion

15. Claims 1-4 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
March 7, 2003

